Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1. (currently amended) A method for designing a candidate polypeptide for expression in a suitable host, said method comprising,

identifying one or more hydrophobic peptide sequences within a polypeptide of interest, and

arranging or re-locating at least one of said hydrophobic peptide sequences within said polypeptide

so as to generate said candidate polypeptide with reduced amplitude in hydrophobicity or length of [[any]] a hydrophobic region[[(s)]].

2. (cancelled).

3. (cancelled).

4. (cancelled).

5. (previously presented) The method of claim 1, wherein the polypeptide of interest comprises a non-natural polypeptide or a theoretical non-natural polypeptide.

6. (previously presented) The method of claim 5, wherein the polypeptide comprises a polyepitope polypeptide comprising a tandem array of epitopes of interest.

7. (currently amended) A method for designing a candidate polyepitope polypeptide comprising a tandem array of epitopes for expression in a suitable host, said method comprising,

identifying the relative hydrophobicity of each of said epitopes,

dividing said epitopes on the basis of said identified hydrophobicities into groups of substantially equivalent numbers, said groups comprising at least a first group of epitopes of most relative hydrophobicity and a second group of epitopes of least relative hydrophobicity, and

arranging epitopes from said first and second groups in a substantially alternating manner so as to generate said candidate polyepitope polypeptide with reduced amplitude in hydrophobicity or length of [[any]] a hydrophobic region[[(s)]].

8. (currently amended) A method for designing a candidate polyepitope polypeptide comprising a tandem array of epitopes for expression in a suitable host, said method comprising,

identifying the relative hydrophobicity of each of said epitopes,

dividing said epitopes on the basis of said identified hydrophobicities into three groups of substantially equivalent numbers, said groups comprising a first group of epitopes of most hydrophobicity, a second group of epitopes of intermediate relative hydrophobicity, and a third group of epitopes of least relative hydrophobicity,

arranging epitopes from said first, second and third groups into triplets containing an epitope from each group, and

arranging said triplets in a linked sequence so as to generate said candidate polyepitope polypeptide with reduced amplitude in hydrophobicity or length of [[any]] a hydrophobic region[[(s)]].

9. (currently amended) A method for designing a candidate polyepitope polypeptide comprising a tandem array of epitopes for expression in a suitable host, said method comprising,

identifying the relative hydrophobicity of each of said epitopes,

dividing said epitopes on the basis of said identified hydrophobicities into four groups of substantially equivalent numbers, said groups comprising a first group of epitopes of most hydrophobicity, a second group of epitopes of lesser relative hydrophobicity, a third group of epitopes of even lesser relative hydrophobicity, and a fourth group of least relative hydrophobicity,

arranging epitopes from said first, second and third groups into quadruplets containing an epitope from each group, and

arranging said quadruplets in a linked sequence so as to generate said candidate polyepitope polypeptide with reduced amplitude in hydrophobicity or length of [[any]] a hydrophobic region[[(s)]].

10. (cancelled).

11. (cancelled).

12. (previously presented) The method of any one of claims 7 to 9, wherein the epitopes comprising the polyepitope polypeptide are selected from epitopes of any one of the viruses of the group consisting of Epstein-Barr virus (EBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and cytomegalovirus (CMV).

13. (previously presented) A method of expressing a polypeptide in a suitable host, said method comprising,

designing a polypeptide in accordance with the method of any one of claims 1, 7, 8, and 9,

introducing a polynucleotide encoding said polypeptide into said host, such that said host is capable of expressing said polypeptide, and

culturing said host under conditions suitable for expression of said polypeptide.

14. (previously presented) A polypeptide designed in accordance with the method of claim 1.

15. (previously presented) A polyepitope polypeptide designed in accordance with the method of claim 1.

16. (previously presented) A polyepitope polypeptide comprising N epitopes, wherein N is any integer, said polyepitope polypeptide having the formula

Triplet 1-Triplet 2-....-Triplet N/3,

wherein each of said triplets comprises three linked epitopes selected by,

identifying and ranking the relative hydrophobicity of each of the N epitopes,

grouping the ranked N epitopes into three groups of substantially equivalent numbers, based upon the identified relative hydrophobicity of the N epitopes, to produce a first group comprising the epitopes of most relative hydrophobicity, a second group of epitopes of intermediate relative hydrophobicity, and a third group of epitopes of least relative hydrophobicity, and

selecting the epitopes for each of said triplets according to the following table:

	Epitope 1	Epitope 2	Epitope 3
Triplet 1 (N-terminal)	Most hydrophilic of Group 2	Most hydrophobic of Group 1	Most hydrophilic of Group 3
Triplet 2	2nd most hydrophilic of Group 2	2nd most hydrophobic of Group 1	2nd most hydrophilic of Group 3
Triplet N/3 (C- terminal)	Most hydrophobic of Group 2	Most hydrophilic of Group 1	Most hydrophobic of Group 3

17. (previously presented) The polyepitope polypeptide of any one of claims 15, 16, 28, 29, and 30, wherein the epitopes are contiguous or spaced apart by intervening sequences which are substantially free of sequences which naturally flank said epitopes.

18. (previously presented) A polypeptide vaccine comprising a polyepitope polypeptide according to any one of claims 15, 16, 28, 29 and 30, and a pharmaceutically acceptable carrier or adjuvant.

19. (previously presented) A polyepitope polypeptide comprising an amino acid sequence substantially corresponding to an amino acid sequence selected from the group consisting of:

FLRGRAYGL-PYLFWLAAI-HRCQAIRKK-RRIYDLIEL-
VQPPQLTLQVGLCTLVAML-RLRAEAQVK-IEDPPFNSL-
YLLEMLWRL-GQGGSPTAMAVLLHEESM-IALYLQQNWWTL-
RAKFKQLL-SSCSSCPLSKI-TYGPVFMCLQAKWRLQTL-
RPPIFIRRL-VSFIEFVGW-YPLHEQHGM-
VEITPYKPTWCLGGLLTMV-EENLLDFVRF-TYSAGIVQI-
LLDFVRFMGV-EGGVGWRHW
(SEQ ID NO : 1),
FLRGRAYGL-PYLFWLAAI-HRCQAIRKK-RRIYDLIEL-
GLCTLVAMLRLRAEAQVK-IEDPPFNSL-TYSAGIVQI-
LLDFVRFMGV-EGGVGWRHWIALYLQQNWWTL-RAKFKQLL-
SSCSSCPLSKI-TYGPVFMCL-QAKWRLQTLRPPIFIRRL-
VSFIEFVGW-YPLHEQHGM-VEITPYKPTW-
CLGGLLTMVEENLLDFVRF-YLLEMLWRL-GQGGSPTAM-
AVLLHEESM-VQPPQLTLQV
(SEQ ID NO : 2),
SSCSSCPLSKI-HRCQAIRKK-CLGGLLTMV-LTAGFLIFL-
RLRAEAQVK-IEDPPFNSL-LLSAWILTA-RRRWRRLTV-
PYLFWLAAI-YLLEMLWRL-GQGGSPTAM-VMSNTLLSAW-

ALLVLYSFA-RAKFKQLL-IALYLQQNW-TYGPVFMCL-

QAKWRLQTL-YLQQNWWTL-YPLHEQHGM-CPLSKILL

(SEQ ID NO : 3),

IPIVAIVALV-RLRPGGKKK-ILKEPVHGV-PLVKLWYQL-

RPGGKKKYKL-KYKLKHIVW-TWETWWTEYW-EIKDTKEAL-

KRWIILGLNK-KLWVTVYYGV-KIEELRQHL-MTNNPPIPV-

VTLWQRPLV-WASRELERF-LLWKGEGAV-YTAFTIPSI-

IYQEPFKNLK-SLYNTVATL-AIIRILQQL-AIFQSSMTK-

VIYQYMDDL-LVGPTPVNI-TPQDLNTML-YLAWVPAHK-

ALVEICTEM-TLNAWVKVV

(SEQ ID NO : 4), and

LLFNILGGWV-KTSERSQPR-FLLLADARV-LLFLLLADA-

RLGVRATRK-GVAGALVAFK-LPGCSFSIF-RMYVGGVEHR-

VAGALVAFK-DLMGYIPLV-LIFCHSKKK-ILAGYGAGV-

HMWNFISGI-QLFTFSPRR-VGIYLLPNR-FWAKHMWNF-

YLVTRHADV-LSAFSLHSY-WMNRLIAFA-YLLPRRGPRL-

YLVAYQATV-RLIVFPDLGV-TLGFGAYMSK-IPFYGKAI-

VLVGGVLAA-CTCGSSDLY

(SEQ ID NO : 5).

20. (previously presented) The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

FLRGRAYGL-PYLFWLAAI-HRCQAIRKK-RRIYDLIEL-VQPPQLTLQV-GLCTLVAML-RLRAEAQVK-IEDPPFNSL-YLLEMLWRL-GQGGSPTAM- AVLLHEESM-IALYLQQNWWTL-RAKFKQLL-SSCSSCPLSKI-TYGPVFMCL-QAKWRLQTL-RPPIFIRRL-VSFIEFVGW-YPLHEQHGM-VEITPYKPTW-CLGGLLTMV-EENLLDFVRF-TYSAGIVQI-LLDFVRFMGV-EGGVGWRHW (SEQ ID NO : 1).

21. (previously presented) The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

FLRGRAYGL-PYLFWLAAI-HRCQAIRKK-RRIYDLIEL-GLCTLVAML-RLRAEAQVK-IEDPPFNSL-TYSAGIVQI-LLDFVRFMGV-EGGVGWRHW-IALYLQQNWWTL-RAKFKQLL-SSCSSCPLSKI-TYGPVFMCL-QAKWRLQTL-RPPIFIRRL-VSFIEFVGW-YPLHEQHGM-VEITPYKPTW-CLGGLLTMV-EENLLDFVRF-YLLEMLWRL-GQGGSPTAM-AVLLHEESM-VQPPQLTLQV (SEQ ID NO : 2).

22. (previously presented) The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

SSCSSCPLSKI-HRCQAIRKK-CLGGLLTMV-LTAGFLIFL-RLRAEAQVK-IEDPPFNSL-LLSAWILTA-RRRWRRLTV-PYLFWLAAI-YLLEMLWRL-GQGGSPTAM-VMSNTLLSAW-ALLVLYSFA-RAKFKQLL-IALYLQQNW-TYGPVFMCL-QAKWRLQTL-YLQQNWWTL-YPLHEQHGM-CPLSKILL (SEQ ID NO:3).

23. (previously presented) The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

IPIVAIVALV-RLRPGGKKK-ILKEPVHGV-PLVKLWYQL-RPGGKKKYKL-KYKLKHIVW-TWETWWTEYW-EIKDTKEAL-KRWIILGLNK-KLWVTVYYGV-KIEELRQHL-MTNNPPIPV-VTLWQRPLV-WASRELERF-LLWKGEGAV-YTAFTIPSI-IYQEPFKNLK-SLYNTVATL-AIIRILQQL-AIFQSSMTK-VIYQYMDDL-LVGPTPVNI-TPQDLNTML-YLAWVPAHK-ALVEICTEM-TLNAWVKW (SEQ ID NO : 4).

24. (previously presented) The polyepitope polypeptide of claim 19, wherein the polyepitope polypeptide comprises an amino acid sequence substantially corresponding to:

LLFNILGGWV-KTSERSQPR-FLLLADARV-LLFLLLADA-RLGVRATRK-GVAGALVAFK-LPGCSFSIF-RMYVGGVEHR-

VAGALVAFK-DLMGYIPLV-LIFCHSKKK-ILAGYGAGV-HMWNFISGI-QLFTFSPRR-VGIYLLPNR-FWAKHMWNF-YLVTRHADV-LSAFSLHSY-WMNRLIAFA-YLLPRRGPRL-YLVAYQATV-RLIVFPDLGV-TLGFGAYMSK-IPFYGKAI-VLVGGVLAA- CTCGSSDLY (SEQ ID NO : 5).

25. (previously presented) A polypeptide vaccine comprising a polyepitope polypeptide according to claim 19 and a pharmaceutically acceptable carrier or adjuvant.

26. (previously presented) A viral or DNA vaccine comprising a polynucleotide encoding a polypeptide designed in accordance with the method of any one of claims 1, 7, 8, and 9 and a pharmaceutically acceptable carrier or adjuvant.

27. (previously presented) A viral or DNA vaccine comprising a polynucleotide encoding a polypeptide according to claim 19 and a pharmaceutically acceptable carrier or adjuvant.

28. (previously presented) A polyepitope polypeptide designed in accordance with the method of claim 7.

29. (previously presented) A polyepitope polypeptide designed in accordance with the method of claim 8.

30. (previously presented) A polyepitope polypeptide designed in accordance with the method of claim 9.